

REMARKS

A. Claims' Amendments

Claims 100, 127, 212, and 412 have been amended to define the Applicants' invention with more precision and particularity. The claims, as amended, are supported by the specification and the original claims. No new matter have been added. For example, support for the limitation "the substance being in a gaseous form at ambient conditions," as recited in claims 100, 127, and 412 is found throughout the specification. See, e.g., page 44, lines 3-20 of the specification. The Applicants further amended Claim 212 to clarify the dependency.

Responding to the Examiner's request for clarification, the Applicants advise the Examiner that claims 301, 302, 304-309, 330, and 338-346 were canceled in the communication filed by the Applicants on January 15, 2001. Upon entry of the amendments, claims 100, 102-103, 127, 194-200, 203, 210-228, 294-300, 303, 310-329, 331-337, 347-356, and 412 are pending.

B. First Rejection Under 35 U.S.C. § 103(a)

The Examiner rejected claims 100, 102-103, 127, 194-200, 203, 210-220, 294-300, 303, 310-317, 326-337, 347-350, and 412 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Grinstaff (U.S. Patent No. 5,498,421) in view of Wallach (U.S. Patent No. 4,853,228), and Allen (U.S. Patent No. 5,620,689) (item 3 on page 3 of the Office Action); or alternatively over Grinstaff in view of Wallach and Allen, and further in view of Schneider (U.S. Patent No. 5,643,553) and Porter (U.S. Patent No. 5,648,098) (item 4 on page 5 of the Office Action); or alternatively over Grinstaff in view of Wallach and Allen, and further in view of Ginsburg (U.S. Patent No. 5,656,442) (item 5 on page 8 of the Office Action). It is respectfully submitted that none of the cited

references, either alone or in combination, disclose or suggest the formulations and methods set forth in the claims submitted herewith.

Each of claims 100, 127, and 412, as amended, requires vesicles comprising "one or more membranes defining an internal void that contains a substantially insoluble substance, the substance being in a gaseous form at ambient conditions."

The Examiner asserted that the substances disclosed by Grinstaff are such that their "characteristics are functional and inherent to the nature of the gas..." (Item 7, page 10 of the Office Action). The Applicants respectfully disagree and point out that what is taught by Grinstaff are liquids at ambient conditions, not gases. The limitation "the substance being in a gaseous form at ambient conditions," recited in claims 100, 127, and 412 is not met by Grinstaff. None of the cited references, either alone or when considered together cure this deficiency, because they do not teach or suggest a formulation including vesicles that include substantially insoluble gases. Indeed, the primary reference, Grinstaff, teaches only encapsulation of liquids, such as highly fluorinated compounds having relatively high molecular weight e.g., perfluoroindane, perfluoromethyl adamantane, perfluorooctyl bromide, perfluorodimethyl cyclooctane, perfluoro cyclooctyl bromide, or perfluoro crown ethers.

Accordingly, it is respectfully submitted that claims 100, 127 and 412 are patentably distinguishable over the references cited by the Examiner. All other claims depend, directly or indirectly, on either claim 100 or claim 127, and are allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

C. Second Rejection Under 35 U.S.C. § 103(a)

In Item 6 on page 9 of the Office Action, the Examiner rejected claims 100, 102-103, 127, 194-200, 203, 210-228, 294-300, 303, 310-329, 331-337, 347-356, and 412 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wallach and Allen in view of Schneider and Porter, and further in view of Ginsburg. The Examiner has stated that one having ordinary skill in the art would have combined the use of liposomes (teachings of Wallach and Allen) with the attaching to a target (Ginsburg) with using a gas (Shneider) with using a perfluorinated gas (Porter). It is respectfully submitted that these references cannot be properly combined for the following reasons.

To establish a *prima facie* case of obviousness, there must be some motivation or suggestion to modify or combine the references. It is axiomatic, that such motivation or suggestion must be found in the references themselves, and the combined references must teach every limitation of the claim. The Applicants submit that in references in question one cannot find motivation or suggestion to combine them, and, even if the references are combined, the combination does not disclose every limitation of claims 100, 127, and 412.

Claims 100, 127, and 412 recite "targeted gas-filled vesicle," which is a membrane defining a cavity filled with gas. The Shneider reference, however teaches "microbubbles" of air or other gases. Shneider specifically defines the microbubbles as air or gas globules suspended in a liquid. See, Shneider, Col. 1, lines 28-29. Shneider further distinguishes his microbubbles as essentially different from the "microcapsules," the former having the gas/liquid interface, while the latter having "a gas entrapped inside solid membrane vesicles." Col. 1, lines 38-40. Moreover, Shneider teaches that the microbubbles are so different from microcapsules, that they "belong to a different kind of art." Col. 1, line 41. Thus, by unambiguously distinguishing the microbubbles and microcapsules, Shneider actually teaches away from using the microcapsules. Since the

vesicles of the present invention include a solid membrane, they are akin to the microcapsules which Shneider teaches are different from the microbubbles. It is indisputable that there is no motivation or suggestion to use the vesicles.

It is, therefore, clear that Shneider does not teach the "gas-filled vesicles" recited in claims 100, 127, and 412 of the present invention. Wallch, Allen, Ginsburg, and Porter, either alone or in combination, fail to cure this deficiency. Accordingly, it is respectfully submitted that claims 100, 127 and 412 are patentably distinguishable over the combination of Wallach, Allen, Schneider, Porter, and Ginsburg cited by the Examiner. All other claims depend, directly or indirectly, on either claim 100 or claim 127, and are allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

In re Application of:
Unger et al.
Application No.: 09/218,660
Filed: December 22, 1998
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PATENT
Attorney Docket No.: IMARX1100-3

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: May 14, 2004

A handwritten signature in cursive script, reading "Lisa A. Haile", written over a horizontal line.

Lisa A. Haile, J.D., Ph.D.
Registration No. 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

USPTO Customer Number 28213
GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133